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EXAMINER

IBRAHIM, MEDINA AHMED

ART UNIT PAPER NUMBER

1638

DATE MAILED 10/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/817,762

Applicant(s)

SPALDING ET AL.

Examiner

Medina Ibrahim

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 July 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 9-14, 17-24 and 27-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 9-14, 17-24 and 27-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application. (See 37 CFR 1.55(a)(2) and 1.56(a)(2)).

* If the claim(s) for foreign priority is/are not accepted, the applicant must file a statement explaining the reasons therefor.

- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1. ☐ Information Disclosure Statement (IDS) filed on _____.
2. ☐ Statement of Inventorship filed on _____.
3. ☐ Statement of Inventorship filed on _____.
4. ☐ Statement of Inventorship filed on _____.

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DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, 1-6, 9-14, 17-24 and 27-31, in Paper No. 9 is acknowledged. The traversal is on the ground(s) that SEQ ID NO:1 and 10 are related in that SEQ ID NO:1 is a cDNA of the gene of SEQ ID NO:10 and examining them together will not place an undue burden on the Examiner. Applicant's arguments have been considered and found persuasive. Therefore, SEQ ID NO:1 and 10 are hereby rejoined. The restriction is made FINAL.

Claims 1-6, 9-14, 17-24, and 27-31 are pending and are under examination.

Sequence Listing

Applicant's CRF and paper sequence listing have been entered.

Information Disclosure Statement

Initialed and dated copy of Applicant's IDS form 1449, Paper No 4 is attached to the instant Office action.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is

Objections

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The disclosure is objected to because it contains an embedded hyperlink. For example, page 8, line 19, cites hyperlink directed to an Internet address. The use of hyperlinks and/or other forms of browser-executable code are not permitted under USPTO current policy. Therefore, Applicant is required to delete the embedded hyperlink. See MPEP § 608.01.

The disclosure is also objected to because figs 5, 6, and 7 are not described in the Brief Description of the Drawings. Correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

3. Claims 1-6, 9-14, 17-24 and 30-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1 and 2, "NPPB" is not descriptive, and therefore, what is encompassed in the claims is unclear. Dependent claims 3-6 and 20-24

In claim 2, it is unclear how the "preferentially expressed" is different from "expressed".

Claim 3 reads as if the plant is 3850-4150 nucleotides long. This does not seem to be Applicants' intention. It is suggested that the second "and" is replaced with ----,

In claim 3, "cDNA" should be replaced with "DNA". The structure is not a cDNA.

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In claim 9, "A" should be changed to ---An--, for proper article; also "a *pIPAC* gene coding sequence--- is unclear. If Applicant intends ---the coding sequence of a *pIPAC* gene---, then the claim should be recited so.

In claims 11 and 12, "in which" should be changed to ---wherein---, for clarification.

Claims 17-19 are indefinite for depending upon cancelled claim 15. Correction is required.

In claim 18, a "reproductive unit" is unclear. Also "form" should be changed to ---from---.

In claims 18 and 19, it is unclear if the "reproductive unit" and "cell" also contain the transgene from the transgenic plant. Applicants should note that due to chimerism, not all of the cells from a transgenic plant will comprise in their genome the transgene construct. In order for the claims not to read the product of nature, it is suggested that --
-transformed--- be inserted after "A".

In claim 20, "the nucleic acid molecule" lacks antecedent basis in claim 1.

In claims 20 and 28, it is unclear how a nucleic acid molecule is operably linked to a vector.

Clarification

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The metes and bounds of claim 24 are unclear because a " nucleic acid molecule of at least 20 nucleotides in length" cannot have a sequence of SEQ ID NO:1 or 10. It is unclear if Applicant intends to claim sequences of at least 20 nucleotides in length from SEQ ID NO:1 or 10, the claim should be recited as such. Also, In parts (c) and (d), ---nucleic acid --- should be inserted before "sequence", for clarification. Also, "regions" should be changed to ---region---. Dependent claims 27-31 are included in the rejection.

Claims 24 and 27 are indefinite for failing to recite specific conditions required for moderate stringency. Also, --conditions-- should be inserted after "stringency", for clarification. The claims recite % "homologous" "identical", "similar" which the specification makes no clear distinction. The claims also recite "at least about x%" of homology. The claims are replete with vague and indefiniteness. Careful and complete review of the claims are suggested.

Claim 27 does not further limit claim 24.

Claim Rejections - 35 U.S.C. § 112, Scope of Enablement

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to make and use the same, and to identify the invention with which it is most nearly

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5. Claims 1-4, 9-14, 17-24 and 27-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated nucleic acid molecule of SEQ ID NO:1 or 10 encoding SEQ ID NO:2, an expression cassette comprising said nucleic acid molecule operably linked to a promoter, a vector comprising said expression cassette, a plant or a plant cell transformed with said vector, does not reasonably provide enablement for any nucleic acid encoding any plant p-glycoprotein that is inducible by exposure of the plant to NPPB or a nucleic acid molecule of at least 20 nucleotides in length and having a sequence of SEQ ID NO:1 or 10 or a sequence having at least 60% homologous thereof or a sequence that hybridizes to SEQ ID NO:1 or 10 or a part thereof under undefined moderate stringency conditions, or a sequence encoding an amino acid sequence that is at least about 40%, 70% or 80% identical to SEQ ID NO:2 or a part thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants broadly claim a nucleic acid molecule from any plant source, including those from *Arabidopsis thaliana* and *Brassica napus*, encoding any p-glycoprotein that is inducible by exposure of the plant to NPPB, as well as fragments of cells, yeast cells, and bacteria cells expressing said nucleic acid molecule as claimed. In contrast, the instant specification provides guidance for the nucleic acid

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molecule from *Arabidopsis thaliana*, designated as ATPAC gene, which encodes the p-glycoprotein of SEQ ID NO:2 which is identified by its upregulation in response to treatment of the plant with 5-nitro-2-(3-phenylpropylamino) benzioc acid (NPPB). The specification disclosed transformed cells and plants expressing said sequences and that the expression of SEQ ID NO:2 in plants is useful in that it protects the plants from the detrimental effects of xenobiotic compounds such as herbicides and other hydrophobic compounds. However, the specification does not provide guidance for pIPAC genes from other plant sources or nucleic acid molecules which encode a p-glycoprotein, other than SEQ ID NO:1 and 10

In re Wands factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims

The instant specification does not provide guidance for how to make and use all
been provided for any modification to SEQ ID NO:1 and 10 that resulted in a molecule
molecules with as low as 60% homology to SEQ ID NO:1 or 10 and still encoding a

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polypeptide that retains p-glycoprotein activity. It is unlikely that the sequence will retain p-glycoprotein activity, if the 40% lack of homology falls in a region responsible for the protein activity. A nucleic acid molecule encoding an amino acid sequence that is at least 70% identical, 40% or 80% similar to SEQ ID NO:2 or residues thereof include those obtainable by modifications such as additions, deletions, and substitutions of one or more amino acids. Applicant has provided no guidance as to which region in SEQ ID NO:2 can be modified so as the protein activity is retained. It is unpredictable as to whether any amino acid substitutions, additions, or deletions in SEQ ID NO:2 will result in desired protein activity. The prior art as exemplified by Lazar et al. (Molecular and Cellular Biology, March 1988, Vol. 8, No. 3, pp. 1247-1252 (U)) and Broun et al. (Science, 13 November 1998, Vol. 282, pp. 131-133 (V)), teach unpredictability in DNA/protein function when one or more amino acids/base in that protein is modified. Lazar et al teaches a mutation of aspartic acid 47 and leucine 48 of a transforming growth factor alpha results in different biological activities (Title). Broun et al teaches as few as four amino acid substitutions can change an oleate 12-desaturase activity (Abstract). Regarding hybridizing sequences, it is noted that nucleic acid sequences that hybridize to SEQ ID NO:1 or 10 under unspecified conditions encode unrelated proteins. The specification does not disclose any relationship between the disclosed p-glycoprotein genes. Therefore, it is unpredictable as to whether one skilled in the art

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can obtain and use the claimed nucleic acid sequences without undue experimentations, absent further guidance.

Therefore, given the state of the art; the nature of the invention; claim breadth; unpredictability; the limited working examples; and the lack of guidance as discussed above, the instant could not be practiced without undue experimentation.

See Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021 and 1027, (Fed. Cir. 1991) at page 1021, where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g a DNA sequence) and page 1027, where it is taught that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof. In this case, the disclosure of SEQ ID NO: 1 or 10 encoding SEQ ID NO:2 does not enable claims drawn to any plant PAC gene or other p-glycoprotein genes or any analog thereof.

Written Description

Claims 1-4, 9-14, 17-24 and 27-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

Claims are broadly drawn to any plant p-glycoprotein genes or any analog thereof. Arabidopsis thaliana and Brassica napus, a multitude of sequences with 60%

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homology, 70% identity, 40% or 80% similarity to SEQ ID NO:1-2, 10 or fragments thereof as well as hybridizing sequences thereof having no known activity. In contrast, the specification only provides guidance for the isolated nucleotide sequence of SEQ ID NO:1 or 10 encoding SEQ ID NO:2. The specification does not describe specific chemical or physical characteristics for all plant p-glycoprotein genes or proteins which would allow one skilled in the art to predictably determine what will be the structure of the non-disclosed sequences. A review of literature does not indicate that such characteristics would be well known by an skilled artisan. While sequences of claims 24 and 27 recite structural limitations such as % of identity, %similarity, %homology or fragment/residues of the disclosed sequences, no functional limitation has been recited in the claims. Therefore, the written description requirement is not satisfied. Therefore, a person skilled in the art would not recognize from the disclosure that Applicant was in possession of the invention as broadly claimed. See, Written Description Examination Guidelines published in Federal Registry/Vol. 66, No. 4/Friday, January 5, 2001/Notices). See, also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an encode the protein from that organism. Despite the disclosure of a cDNA encoding a protein from another organism.

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Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 24 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Lansing (Plant physiology, vol. 106, pp.1241-1255, 1994)

The claims are directed to an isolated nucleic acid molecule of at least about 20 nucleotides in length having a sequence which is at least about 60% homology to SEQ ID NO:1 or 10, or an oligonucleotide of about 10 and about 100 nucleotides in length hybridizing a portion thereof at moderate stringency, a sequence encoding an amino acid sequence that is at least 70% identical, 40% or 80% similar to SEQ ID NO:2 or a part thereof.

Lansing teaches isolated nucleotide sequences from *Arabidopsis thaliana* having 140 contiguous nucleotides of SEQ ID NO:1 with 100% sequence similarity and which will inherently encode and will hybridize under stringency conditions to SEQ ID NO:1 or a part thereof (Sequence Search Results, pages 7-8, Accession No. AA394594).

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Deposited 1997). Applicants note the claimed nucleotide sequences not necessarily be contiguous.

Remarks

SEQ ID NO:1 or 10 encoding SEQ ID NO:2 are free of the prior art of record.

Claim 5 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 6 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Papers relating to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (703) 306-5822. The Examiner can normally be reached Monday -Tuesday from 8:00AM to 4:00PM and Wednesday-Thursday from 9:00AM to 3:00 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218.

Any inquiry of a general nature or relating to the status of this application should

September 25, 2002